REMARKS

Claims 1 to 4 and 14 are pending. Claims 5 through 13 are canceled. Claim 14 is new. Applicant reserves the right to pursue the canceled claims in a divisional application. No new matter is added.

Support for new claim 14 may be found throughout the application and, for example, in claim 1 as originally filed, which was directed to a process for stimulating the immune system of a subject to release antimalignin antibody comprising administering to the subject an effective amount of a first dosage of a composition comprising Recognin M, or other peptides having the immunological specificity of Recognin M, such as malignin and Recognin L. The specification teaches that Recognin M shares "immunological specificity" with malignin and Recognin L. Spec. at 17.

Further support may be found for new claim 14, for example, in the specification, which teaches that Recognin M and malignin are peptides of about 10 kDa with identical immunoreactivity wherein malignin was produced from glioblastoma cells and Recognin M was produced from MCF7 breast cancer cells. *See* Spec. at 5-6 (bridging paragraph). The specification further teaches that anti-Recognin antibodies such as antimalignin and anti-Recognin M antibodies bind to a range of cancer cells *in vitro* (Example 1), bind to a range of cancer cells in humans *in vivo* (Example 2), inhibit growth of small cell lung carcinoma cells *in vitro* (Example 6), increase in concentration in humans with age and with the presence of breast cancer (Example 7 at page 15 and Figure 3), and may be administered subcutaneously to a subject in doses of approximately 1 mg or more to induce an immune response (Example 8).

In particular, Example 8 teaches that a Recognin derivative vaccine can be any product that contains "the immunological specificity of malignin, Recognin L or Recognin M." Spec. at 17. In Example 8, the specification incorporates by reference U.S. Patent No. 4,976,957, which teaches that "malignin, astrocytin, Recognin M and Recognin L are [all] Recognins." Col. 7, ll. 2-3. The patent further teaches that antibodies and other chemoreciprocals of Recognins react with immunochemical-like specificity with the family of Recognins. Col. 1, ll. 24-36.

As such, claim 1 as originally filed and the specification throughout provide support for new claim 14. New claim 14 contains no new matter.

Enablement Rejection of Claims 1-4

1. The enablement rejection is based on a misunderstanding of the size of Recognin peptides

In the final Office Action mailed September 24, 2007, the Office maintains an enablement rejection of claims 1-4 because Example 8 in the specification allegedly "teaches one how to stimulate production of anti-recognin antibody, not of anti-malignin antibody." Office Action at 2. The Office alleges that "Recognin is a 250,000 Dalton glycoprotein that is a precursor of malignin" and that "malignin is inherently a 16-mer peptide of much lower molecular weight." The Office concludes from the asserted molecular weights of the compounds that while"[o]ne of skill would expect a macromolecule of such molecular weight [like Recognin] to be immunogenic" one of skill "would not expect a peptide of such lower molecular weight [such as malignin] to be immunogenic." The Applicant respectfully traverses the Office's conclusion concerning the molecular weights of Recognin and malignin and further respectfully traverses the Office's understanding of the identity of the Recognin and malignin peptides.

Contrary to the Office's allegations, Recognins are a family of peptides having molecular weights of about 8 to about 10 kDa. *See* Spec. at 5-6 ("When malignin was produced as the immunogenic fragment of the precursor it was thought to be a cell-type-specific cancer marker. It was only when similar 10K peptides with identical immunoreactivity were produced from MCF7 breast cancer cells (Recognin M) and from P3J lymphoma (Recognin L) that malignin appeared to be a more general cancer antigen.") Recognins are not the 250 kDa precursor of Malignin. Rather Recognin defines a family of peptides of about 10 kDa that includes malignin. The specification teaches that Recognins are all about 10 kDa, all share immunoreactivity, and all generate anti-Recognin antibodies that are similarly immunoreactive with the family of Recognin peptides. *See* Spec. at 17 and U.S. Pat. No. 4,976,957 cols. 1-3. Because the Office has misread the specification and has made unsubstantiated allegations concerning the data provided in the specification, the Applicant respectfully requests the Office withdraw its rejection of claims 1-4.

The specification specifically teaches that malignin, Recognin M and Recognin L share immunological specificity. Spec. at 17. The specification further incorporates U.S. Patent No. 4,976,957 by reference when describing malignin, Recognin L and Recognin M. Spec. at 17.

U.S. Patent No. 4,976,957 expressly teaches that "malignin, astrocytin, Recognin M and Recognin L are [all] Recognins." Col. 7, ll. 2-3. The patent further teaches Astrocytin is an about 8 kDa Recognin (col. 1, ll 37-38, 65), Recognin M is an about 8 kDa Recognin (col. 3, ll. 8-16), Recognin L is an about 8 kDa Recognin (col. 3, ll. 25-33) and malignin is an about 10 kDa Recognin (col. 2, ll. 32-39). For example, U.S. Patent No. 4,976,957 states concerning the isolation of malignin: "In a manner similar to that described above, another Recognin, called Malignin, is produced from artificial cancer cells, i.e., cancer cells grown in *in vitro* fermentation. Malignin has a molecular weight of about 10,000 and similar but distinct amino acid residue composition to Astrocytin . . . ." *Id.*, col. 2, ll. 32-39.

The Office further erroneously alleges that Example 8 of the specification teaches production of an antibody to a 250 kDa peptide. The Office is wrong. Example 8 teaches the production of anti-malignin antibodies by subcutaneous administration of malignin, a 10 kDa peptide, not by administration of the 250 kDa precursor of malignin. Example 8 expressly teaches administration of any product that contains the immunological specificity of malignin to produce an immune response to malignin or other Recognin peptide (such as astrocytin). *See* Spec. at 17. The specification then incorporates U.S. Patent No. 4,976,957 by reference. Example 7 of U.S. Patent No. 4,976,957 expressly teaches administration of "1 mg. of Astrocytin or Malignin" injected into the toe pads of white male rabbits to produce antisera to astrocytin or malignin. Col. 24, ll. 16-19. As such, the Office is incorrect to allege that Example 8 does not teach production of anti-malignin antibody.

2. The enablement rejection is based on a misreading of the 1.132 declaration

The Office further finds the 1.132 declaration of Samuel Bogoch, M.D., Ph.D. filed on April 4, 2007 to be "unconvincing" because "Example 5 discloses results obtained with an anti-recognin antibody, not an antimalignin antibody." Office Action at 3. Once again, the Office has reached this conclusion based on a misreading of the specification. The specification establishes that the anti-Recognin antibody of the specification is an antibody against malignin. For example, Example 7 makes clear that the anti-Recognin antibodies of the specification are the same as anti-Malignin antibodies. Spec. at 14 ("Increase in concentration of serum anti-Recognin (antimalignin) antibody . . . ."). Further, U.S. Patent No. 4,976,957 (incorporated by reference) expressly teaches that "malignin, astrocytin, Recognin M and Recognin L are [all]

Recognins." Col. 7, ll. 2-3. The Office, therefore, has again confused the Recognin precursor of 250 kDa with Recognins, namely peptides of about 10 kDa that share immunospecificity.

Example 5 states that in Figures 1j through 1l, cytotoxicity may be observed from application of anti-Recognin antibodies. As may be seen on page 8 of the specification and in Figures 1j through 1l, *in vitro* killing of glioblastoma brain cancer cells with application of anti-Recognin antibody is demonstrated. The "anti-Recognin" antibody on page 8 is antibody that was eluted from malignin peptide of 10 kDa, not a peptide of 250 kDa. Spec. at 11 ("The final preparation contained malignin with the following composition . . . . demonstrating a molecular weight of approximately 10K . . . .").

3. Antimalignin antibodies were observed bound to the brain of Wistar rats and were observed to kill glioblastoma cells in vitro

The Office further questions whether the specification shows anti-malignin antibodies bound to glioblastoma cells in Wistar rats. In Example 2, the specification teaches that "anti-Recognin given intravenously has been shown to bind preferentially to malignant glioma cells in the rat brain *in vivo*." Spec. at 9. The specification cites Bogoch *et al.*, Protides of Biological Fluids 30, 337-352 (1983) as demonstrating the preferential *in vivo* binding of antibody in rat brain. Spec. at 9, fn. 7. The 1.132 Bogoch declaration cites the very same article at paragraphs 10 and 11 in support of its statement that *in vivo* binding has been observed in rat brain. The declaration further attaches the article as Tab D wherein *in vivo* binding is reported at page 349. Bogoch *et al.*, Protides of Biological Fluids 30, 337-352 (1983) As such, there can be no doubt that anti-malignin antibody has been observed to bind to glioblastoma cells in rat brain *in vivo*.

The Office also alleges that while the 1.132 Bogoch declaration refers to Example 1 as showing that anti-malignin antibody is cytotoxic to glioblastoma brain cancer cells, Example 1 instead shows "that anti-malignin antibody is able to immunocytochemically stain, rather than kill, cancer cells." Office Action at 4. Again the Office is mistaken. Example 1 expressly teaches "cytotoxicity of 50 microliters of anti-Recognin antibody, 10 micrograms/mL, left in contact for varying periods of time with glioblastoma brain cancer cells" shown in Figures 1j through 1l. Spec. at 8. Figures 1j, 1k and 1l demonstrate varying degrees of cell killing based on increased time of action of the anti-malignin antibodies.

The Office further alleges Example 6 does not show inhibition of the growth of cancer cells by anti-malignin antibody. Again the Office has misread the specification. As

demonstrated above, anti-Recognin antibody is antimalignin antibody. *See* Spec. at 14 ("Increase in concentration of serum anti-Recognin (antimalignin) antibody . . . ."). Example 6 demonstrates inhibition of growth of small cell lung cancer with administration of antimalignin antibody.

4. Applicant has demonstrated immune stimulation with malignin

The Office further alleges that "cancer vaccines don't work" because, for example, the specification "has not taught how the 16-mer peptide that constitutes malignin might be better presented in the context of MHC molecules, how it might be better presented by dendritic cells, or how it might be combined with a better adjuvant." Office Action at 5-6. The Applicant respectfully traverses the Office's allegation. As established above, malignin is not a 16-mer peptide. It is much larger at about 10 kDa. Further, the specification provides examples of the production of antibodies to malignin via subcutaneous administration of the malignin peptide. U.S. Patent No. 4,976,957, col. 24, ll. 16-19 (incorporated by reference at page 17) (expressly teaching administration of "1 mg. of Astrocytin or Malignin" injected into the toe pads of white male rabbits to produce antisera to astrocytin or malignin). As such, malignin does not need to be better presented to the immune system to stimulate the immune response of the claims. Malignin has already been shown to stimulate the immune system on its own after subcutaneous administration. *See, e.g.*, U.S. Patent No. 4,976,957, Example 7.

4. The enablement rejection has been obviated

As demonstrated above, the Office's rejection of claims 1-4 is based on (1) a misunderstanding of the 10 kDa malignin peptide in the specification, (2) a misunderstanding of the size of about 10 kDa Recognin peptides, (3) a misstatement concerning the Applicant's actual production of antimalignin antibodies via subcutaneous administration of malignin oncoprotein, and (4) a refusal to acknowledge the express specification teaching that the Applicant has shown actual killing of glioma cells using antimalignin antibodies. Because the Applicant has disclosed a method for killing glioma cancer cells in a subject comprising administering an effective amount of a first dosage of a composition comprising malignin that stimulates the immune system to produce and release antimalignin antibody that binds and kills glioma cancer cells, and has enabled the method so that one of skill in the art may simply subcutaneously administered malignin in a subject with glioma cancer cells to practice the

method, the Applicant respectfully requests the Office withdraw the enablement rejection of claims 1-4.

Request for Interview

The Applicant respectfully requests an in-person interview with Examiner Saunders and Supervisory Examiner Chan prior to substantive action in response to the present filing. The Applicant believes an in-person interview will help clarify issues that have arisen in this application.

CONCLUSION

It is believed that the present claims are in condition for allowance and Applicant earnestly requests the same. An early and favorable action on the merits is earnestly solicited. The Examiner is invited to contact the undersigned attorney at 202-220-4268 to expedite allowance.

The Commissioner is authorized to charged any fees or overpayments associated with this application to Kenyon & Kenyon LLP **Deposit Account No. 11-0600**.

Respectfully submitted,

KENYON & KENYON LLP

/Richard W. Ward/

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